Remarks

As a preliminary matter, applicant acknowledges that the previous rejections of the claims, and in particular, claims 1-4, 6-9, 17-20, and 22-28, have been withdrawn in view of applicant's response filed March 13, 2003.

Claims 1-7 and 17-29 were pending. By way of this response, claims 1, 17, and 26 have been amended, and claim 27 has been cancelled. Support for the amendments to the specification and the claims can be found in the application as originally filed, and no new matter has been added. Accordingly, claims 1-7, 17-26, and 28-29 are currently pending.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-9 and 17-26 have been rejected under 35 U.S.C. § 112, second paragraph. In particular, the Examiner believes that the claims are unclear or indefinite for reciting "... to control a duration of therapeutic activity."

Applicant respectfully traverses the rejection.

As applicant has previously indicated in the response filed September 27, 2001, the United States Board of Patent Appeals and Interferences has addressed this issue in the parent application, U.S. Serial No. 08/075,032, and has determined that the claims reciting the language "... to control a duration of therapeutic activity" **are definite** under 35 U.S.C. § 112, 2nd paragraph. At page 7 of the Decision on Appeal for U.S. Serial No. 08/075,032, the Board reversed the Examiner's rejection, and

agreed with applicant that the phrase "to control a duration of therapeutic activity" is definite. Thus, applicant respectfully requests the Examiner to withdraw the rejections. The relevant page from the Board's decision is enclosed.

In view of the above, applicant submits that the claims satisfy the requirements of 35 U.S.C. § 112, second paragraph, and respectfully requests that the rejection of the present claims based on this statutory provision be withdrawn.

Rejections Under 35 U.S.C. § 103

Claims 1, 6, 17, 22, and 26-27 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Ludlow et al. in view of Schantz et al.; Ludlow et al. in view of Tsui et al.; and Ludlow et al. and Shantz et al. in view of Sugiyama. Claims 1-9 and 17-29 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Ludlow et al. and Shantz et al. in view of Sugiyama.

Applicant respectfully traverses the rejections as they apply to the present claims.

Applicant submits that Office Action has failed to establish a *prima facie* case of obviousness. For example, the Office Action fails to indicate where in the prior art, a suggestion or motivation is provided to modify the teachings of the references to obtain the claimed methods and compositions, which recite compositions containing a combination of two or more specific neurotoxins. The motivation or suggestion to support a rejection under 35 U.S.C. § 103 must be clear and

particular (*In re Dembiczak*, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999); emphasis added), and "particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed" (*In re Kotzab*, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000)). Applicant respectfully submits that the prior art fails to provide a clear and particular showing that one of ordinary skill in the art would have been motivated to modify the teachings of the references to obtain the claimed compositions. Absent such a clear and particular indication, the rejections under 35 U.S.C. § 103 cannot be maintained.

In addition, even if the references could be combined, the combination fails to disclose, teach, or even suggest all of the limitations recited in the present claims, such as each selected neurotoxin being present in an amount selected to control a duration of therapeutic activity of the combination of neurotoxins, as recited in claims 1-7 and 17-26, or the specific combination of botulinum toxin type A and botulinum toxin type B, as recited in claim 28, or the specific combination of botulinum toxin type A and botulinum toxin type E, as recited in claim 29.

The rejections of the claims under 35 U.S.C. § 103 appear to be based on the Examiner's opinion that it would have been obvious to one of ordinary skill in the art at the time of the invention to combine two compositions each containing a single neurotoxin based on the "idea that combining them flows logically from [single neurotoxins] having been individually taught in the prior art," or "the substitution of one

[neurotoxin] for the other would be readily expected to work given that two of the individual neurotoxins have been individually shown to be effective for the treatment of torticollis." The Examiner appears to be of the opinion that because the references teach pharmaceuticals having a single type of botulinum toxin, and that seven different types of botulinum toxin were known, it would have been obvious to one of ordinary skill in the art at the time of the invention to include a combination of botulinum toxins in a composition.

However, as acknowledged in the Office Action, none of the references teach a composition comprising at least two types of botulinum toxins, or the use thereof (see page 3, last paragraph; page 4, first paragraph; and page 5, fifth paragraph).

Applicant submits that the Office Action actually supports the unobviousness of the present invention. As indicated above, the Office Action states that substitution of one neurotoxin for the other would be expected to work. Thus, the Office Action admits that the prior art at best suggests that substitution of one toxin for another, separately, might be expected to work. Substituting one neurotoxin for another is not the same as, and is, in fact, completely different and distinct from combining two neurotoxins. The references taken alone, or in combination, do not disclose, teach, or even suggest that two or more neurotoxins in combination in one composition would be therapeutically effective.

Furthermore, applicant submits that the references alone, or in combination, do not disclose, teach, or even suggest,

compositions which contain a combination of at least two botulinum toxins, each botulinum toxin being present in an amount selected to control a duration of therapeutic activity of the combination of neurotoxins, as recited in claims 1-7 and 17-26. In fact, not only are the references silent as to compositions containing a combination of botulinum toxins, the references are expressly silent with respect to any specific amount of toxins used in a combination, let alone, amounts that are effective to control a duration of therapeutic activity. Thus, because the references individually do not disclose, teach, or even suggest, a composition comprising a combination of botulinum toxins in specific amounts, as recited in the claims, the reference combination contended by the Examiner fails to recite all of the limitations recited in the pending claims, and in particular claims 1-7, and 17-26.

Similarly, the references alone or in combination do not disclose, teach, or even suggest any specific combinations of individual neurotoxins, let alone the specific combination of botulinum toxin type A and type B, as recited in claim 28, or the specific combination of botulinum toxin type A and type E, as recited in claim 29.

In view of the above, applicant submits that the present claims 1-9 and 17-26 and 28-29 are unobvious from and patentable over Ludlow et al., Shantz et al., Tsui et al., and Sugiyama et al., alone or in combination, under 35 U.S.C. 103(a).

Each of the present dependent claims is separately patentable over the prior art. For example, none of the prior art disclose, teach, or even suggest the present methods and

compositions including the additional feature or features recited in any of the present dependent claims, such as the specific combinations of neurotoxins. Therefore, applicant submits that each of the present claims is separately patentable over the prior art.

In conclusion, applicant has shown that the present claims satisfy the requirements of 35 U.S.C. § 112, and are unobvious from and patentable over the prior art under 35 U.S.C. § 103. Therefore, applicant submits that the present claims, that is claims 1-7, 17-26, and 28-29 are allowable. Therefore, applicant requests the Examiner to pass the above-identified application to issuance at an early date. Should any matters remain unresolved, the Examiner is requested to call (collect) applicant's attorney at the telephone number given below.

Respectfully submitted,

Date: OCTOBER 14, 2003

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